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10/766,124	01/28/2004	Jane Hirsh	CP 108	2103

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1609	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,124	HIRSH ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 28* is/are pending in the application.

4a) Of the above claim(s) *11, 16, 23 and 25 - 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 10, 12 - 15, 17 - 22, 24 and 27 - 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *23 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The previous Requirement for Restriction/Election mailed on August 7, 2007 has been vacated. Following is the revised restriction/species election requirement with telephonic election and action on the merits for the elected invention.

Elections

1. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Applicant is required to elect a species from each of the following 5 species election requirements. Applicant is cautioned that election of a specific compound that does not have specific written basis as filed may be determined to be New Matter.

First Species Election Requirement

Applicant is required to elect either embodiments having no specified release formulation or a specified release formulation for the particles. If an embodiment having a particular release formulation for the particles is elected, applicant is further required to elect from those release formulations listed in claims 5 through 10 or a particle formulation not listed in claims 5 through 10.

Second Species Election Requirement

Applicant is required to elect either embodiments with no specified dosage form or a specified dosage form. If a particular dosage form is elected, applicant is further required to elect a dosage form from those listed in claims 11 through 12 or a dosage form not listed in claims 11 through 12.

Third Species Election Requirement

Applicant is required to elect either embodiments with no specific milnacipran side effect or a specific milnacipran side effect with diminished incidence or reduced intensity. If a side effect is elected, applicant is further required to elect a side effect from those listed in claims 14 through 16 or a side effect not listed in claims 14 through 16.

Fourth Species Election Requirement

Applicant is required to elect the embodiments with either the presence or absence of additional active ingredient(s). If their presence is elected, applicant is further required to elect the additional active ingredients from those listed in claim 20 or an active ingredient not listed in claim 20.

Fifth Species Election Requirement

Applicant is required to elect the enantiomeric composition embodiment of the milnacipran from those listed in claims 23 – 26 or an enantiomeric composition not listed in claims 23 – 26.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim

is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Restriction for examination purposes as indicated is proper because all these inventions listed in this action are independent or distinct for the reasons given above and there would be a serious search and examination burden if restriction were not required because one or more of the following reasons apply:

(a) the inventions have acquired a separate status in the art in view of their different classification;

(b) the inventions have acquired a separate status in the art due to their recognized divergent subject matter;

(c) the inventions require a different field of search (for example, searching different classes/subclasses or electronic resources, or employing different search queries);

(d) the prior art applicable to one invention would not likely be applicable to another invention;

(e) the inventions are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention.**

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

2. During a telephone conversation with Patrea Pabst and Cecilia Tsang on August 27, 2007 a provisional election was made to prosecute the invention of the formulation

as in claim 14, with an additional analgesic present, a racemic mixture of milnacipran with a decreased incidence of the side effect of nausea, claims 1 – 10, 12 – 15, 17 – 22, 24 and 27 – 28. Affirmation of this election must be made by applicant in replying to this Office action. Claims 11, 16, 23 and 25 – 26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Status of Claims

Claims 1 – 28 are pending. Claims 11, 16, 23 and 25 – 26 are withdrawn from consideration. Claims 1 – 10, 12 – 15, 17 – 22, 24 and 27 – 28 are under examination.

Claim Rejections - 35 USC § 112 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 21, 22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "therapeutically equivalent dose" and "dosage equivalent" are not defined and it is unclear what is meant by terms.

5. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "defined period of time" has no antecedent basis

in this claim or any of the claims that is depends from and it is unclear what is meant by this limitation.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1 – 10, 12 – 15, 17, 18 and 27 – 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman (US Patent 5,980,882).

Eichman teaches methods of making, compositions and methods of administering a drug to a patient in need of a drug. The drug is provided as a complex of drug with an ion-exchange resin that also comprises a chelating agent for improved stability. Complexation of a drug with a resin can affect the rate of dissolution in the digestive system and often leads to slower dissolution (col 1, ln 41 – 51). Typical particle sizes of the ion-exchange resins range from about 25 to 1000 μm (col 6, ln 65 – 67). Any drug that exists in an ionic form in a semi-polar or polar solvent are potential candidates for complexation with an ion-exchange resins (col 7, ln 7 – 9) but milnacipran is exemplified as a candidate in col 9, ln 38. Coatings to slow the rate of dissolution of the drug-resin complex further in the gastrointestinal tract may be added

(col 12, ln 2 – 64). These coatings may be enteric or any film-forming material with diffusion barrier properties (col 12, ln 65 – col 13 ln 1). These microparticules are applicable not only to solid dosage forms but also for syrups and suspensions (col 13, ln 19 – 21). Methods of making the composition (col 5, ln 38 – 65) and methods of administering to a patient (col 6, ln 32 – 40) are also provided. The claims of the instant application drawn to compositions contain functional language in regards to decreased incidence of side effects. The reduction in side effects is inherent to the compositions.

Given the general teachings of Eichman as to generic controlled release formulations comprising an ion-exchange resin and milnacipran as a suitable drug release candidate, one of ordinary skill in the art at the time of the instant invention would have a reasonable expectation of success in formulating a composition comprising milnacipran and an ion-exchange resin.

8. Claims 1 – 10, 12 – 15, 17, 18, 21, 22, 24, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman as applied to claims 1 – 10, 12 – 15, 17, 18 and 27 – 28 above in view of Paillard et al. (US Patent 6,699,506 B1).

As discussed above, Eichman teaches ion-exchange drug resin compositions but does not disclose the dosages of the drugs used or the stereochemical makeup of drugs with a stereocenter.

Paillard et al. teaches delayed release compositions of milnacipran with a sacchrose or starch core (col 1, ln 35 – 38). Both a once daily dosage, comprising 50 – 240 mg of milnacipran (ln 32 – 33) and a dosage of racemic milnacipran (col 1, ln 49)

are taught by Paillard et al. The minigranules that contain the milnacipran can be coated with a polymer film allowing for altered *in vitro* release profiles, including one in which between 10% and 55% of the dose is released in 2 hours (col 1, ln 38 – 47).

It would have been obvious to one or ordinary skill in the art at the time the invention was made to change the delay release material for the racemic milnacipran from the starch or saccharose of Paillard et al. to the ion exchange resin delayed release formulation taught by Eichman with a reasonable expectation of success.

9. Claims 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eichman and Paillard et al. as applied to claims 1 – 10, 12 – 15, 17, 18, 21, 22, 24, 27 and 28 above in view of Kranzler et al. (US Patent 6,602,911 B2).

Eichman and Paillard et al. teach drug-ion resin compositions with altered drug release properties that can be used with milnacipran and other drugs but does not teach concurrent administration of two different drugs or dosages of the drug to be delivered.

Kranzler et al. discusses treatment of fibromyalgia, chronic fatigue syndrome or pain using compositions of milnacipran (col 2, ln 40 – col 3, ln 16). Concurrent administration of milnacipran with an analgesic compound is taught (col 7, ln 56 – 57).

It would have been obvious to one of ordinary skill in the art to combine the ion-exchange resin based composition with milnacipran with an analgesic with a reasonable expectation of success to arrive at the claims of the instant application.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claim 28 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 27 of copending Application No. 11/192,697 in view of Eichman and Paillard et al.

As discussed above, Eichman teaches methods of making a delayed release formulations of drug-ion exchange resin complexes that may be coated with an additional layer. Paillard et al. teaches a delayed release milnacipran composition comprising a saccharose core that can also be optionally coated with another layer.

It would obvious to one of ordinary of skill to employ the method of making drug-ion exchange resin of Eichman with the delayed release formulation of milnacipran taught by Paillard et al.

This is a provisional obviousness-type double patenting rejection.

12. Claims 1, 8, 13, 15, 20, 21, 22 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 9, 12 and 16 - 18 of copending Application No. 10/690,872 in view of Eichman and Paillard et al.

As discussed above, Eichman teaches methods of making a delayed release formulations of drug-ion exchange resin complexes that may be coated with an

additional layer. Paillard et al. teaches a delayed release milnacipran composition comprising a saccharose core that can also be optionally coated with another layer.

It would obvious to one of ordinary of skill to employ the method of making drug-ion exchange resin of Eichman with the delayed release formulation of milnacipran taught by Paillard et al. Pulsatile release is defined in the instant application as a single dosage form that mimics a multiple dosing profile with at least a two-fold reduction in dosing frequency and is therefore a particular type of delayed release formulation that is obvious over the generic delayed release formulations taught by Eichman and Paillard et al.

This is a provisional obviousness-type double patenting rejection.

13. Claim 27 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 24 of copending Application No. 10/690,947 in view of Eichman and Paillard et al.

As discussed above, Eichman teaches methods of treating a patient with a delayed release formulations of drug-ion exchange resin complexes (col 20, ln 47) that may be coated with an additional layer. Paillard et al. teaches a delayed release milnacipran composition comprising a saccharose core that can also be optionally coated with another layer.

It would obvious to one of ordinary of skill to employ the method of using the drug-ion exchange resin of Eichman with the delayed release formulation of milnacipran taught by Paillard et al. to treat a patient in need of milnacipran.

This is a provisional obviousness-type double patenting rejection.

14. Claims 1, 8, 15, 17, 18 and 20 – 22 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, 5, 9, 12 and 15 - 17 of copending Application No. 10/691,936 in view of Eichman and Paillard et al.

As discussed above, Eichman teaches methods of making a delayed release formulations of drug-ion exchange resin complexes that may be coated with an additional layer. Paillard et al. teaches a delayed release milnacipran composition comprising a saccharose core that can also be optionally coated with another layer.

It would obvious to one of ordinary of skill to employ the method of making drug-ion exchange resin of Eichman with the delayed release formulation of milnacipran taught by Paillard et al.

This is a provisional obviousness-type double patenting rejection.

15. Claims 1, 8, 10, 15, 20, 21 and 24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim1, 2, 9, 11, 14 – 16, and 18 – 19 of copending Application No. 11/192,885 in view of Eichman and Paillard et al.

As discussed above, Eichman et al. teaches methods of making a delayed release formulations of drug-ion exchange resin complexes that may be coated with an

additional layer. Paillard et al. teaches a delayed release milnacipran composition comprising a saccharose core that can also be optionally coated with another layer.

It would obvious to one of ordinary of skill to employ the method of making drug-ion exchange resin of Eichman to arrive at a different delayed release formulation of milnacipran than taught by Paillard et al.

This is a provisional obviousness-type double patenting rejection.

Conclusion

Claims 1 – 10, 12 – 15, 17 – 22, 24 and 27 – 28 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571) 270-3532. The examiner can normally be reached on M - F, 7:30 a.m. - 5 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718 or Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NMW

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